

AMENDMENTS TO THE CLAIMS

The following listing of claims replaces all previous listings of claims:

Claim 1-9 (cancelled)

Claim 10 (Currently amended): A method for screening for biologically active agents that modulate hepatocellular carcinoma development, the method comprising:

administering a candidate agent to a transgenic mouse having a genome comprising a stably integrated transgene encoding FGF19 operably linked to a promoter, wherein said transgene results in said mouse developing hepatocellular carcinoma characterized by increased proliferation of pericentral hepatocytes, or elevated levels of alpha-fetoprotein as compared with a control non-transgenic or transgenic mouse; and

determining the extent of development of the hepatocellular carcinoma as indicated by the extent of proliferation of pericentral hepatocytes, or elevated levels of alpha-fetoprotein of said mouse as compared with [[a]] the control non-transgenic or transgenic mouse.

Claim 11 (Currently amended): A method for screening for biologically active agents that modulate hepatocellular carcinoma development, the method comprising:

administering a candidate agent to a transgenic mouse cell culture, each cell of said culture comprising a stably integrated transgene encoding FGF19 operably linked to a promoter, wherein said transgene results in said mouse developing hepatocellular carcinoma characterized by increased proliferation of pericentral hepatocytes or elevated levels of alpha-fetoprotein as compared with [[the]] a control non-transgenic or transgenic mouse; and

determining the effect of said agent on the transgenic mouse cell culture as indicated by extent of proliferation of the transgenic mouse cell culture.

Claims 12-178 (cancelled)

Claim 179 (previously presented): The method of claim 10, wherein the FGF-19 is expressed in skeletal muscle.

Claim 180 (cancelled)

Claim 181 (Currently amended): The method of claim 10, wherein the extent of development of hepatocellular carcinoma is indicated by the extent of proliferation of pericentral hepatocytes as compared with a control non-transgenic or transgenic mouse.

Claim 182 (previously presented): The method of claim 10, wherein the extent of development of hepatocellular carcinoma is indicated by the levels of alpha-fetoprotein of said mouse as compared with a control transgenic mouse.

Claim 183-186 (cancelled)

Claim 187 (previously presented): The method of claim 10, wherein the agent is an antibody.

Claim 188 (previously presented): The method of claim 10, wherein the agent is a small molecule.

Claim 189 (Currently amended): A method for screening for biologically active agents that modulate hepatocellular carcinoma development, the method comprising:

administering a candidate agent to a transgenic mouse having a genome comprising a stably integrated transgene encoding FGF19 operably linked to a promoter, wherein said transgene results in said mouse developing hepatocellular carcinoma characterized by a liver tumor as compared with a control non-transgenic or transgenic mouse; and

determining the extent of development of the hepatocellular carcinoma as indicated by the liver tumor as compared with the control non-transgenic or transgenic mouse.

Claim 190 (previously presented): The method of claim 189, wherein the FGF-19 is expressed in skeletal muscle

Claim 191 (previously presented): The method of claim 189, wherein the extent of development of hepatocellular carcinoma is indicated by size of the liver tumor.

Claim 192 (previously presented): The method of claim 191, wherein the size of the liver tumor is determined by liver weight.

Claim 193 (previously presented): The method of claim 192, wherein the size of the liver tumor is determined by measuring the liver tumor prior to and after administration of the candidate agent.

Claim 194 (previously presented): The method of claim 189, wherein the liver tumor comprises beta-catenin immunoreactive cells.

Claim 195 (previously presented): The method of claim 189, wherein the agent is an antibody.

Claim 196 (previously presented): The method of claim 189, wherein the agent is a small molecule.

Claim 197 (New): The method of claim 10, wherein the development of hepatocellular carcinoma is selected from the group consisting of growth, proliferation and metastasis of hepatocellular carcinoma.

Claim 198 (New): The method of claim 197, wherein the development of hepatocellular carcinoma comprises growth of hepatocellular carcinoma.

Claim 199 (New): The method of claim 197, wherein the development of hepatocellular carcinoma comprises proliferation of hepatocellular carcinoma.

Claim 200 (New): The method of claim 197, wherein the development of hepatocellular carcinoma comprises metastasis of hepatocellular carcinoma.

Claim 201 (New): The method of claim 11, wherein the development of hepatocellular carcinoma is selected from the group consisting of growth, proliferation and metastasis of hepatocellular carcinoma.

Claim 202 (New): The method of claim 201, wherein the development of hepatocellular carcinoma comprises growth of hepatocellular carcinoma.

Claim 203 (New): The method of claim 201, wherein the development of hepatocellular carcinoma comprises proliferation of hepatocellular carcinoma.

Claim 204 (New): The method of claim 201, wherein the development of hepatocellular carcinoma comprises metastasis of hepatocellular carcinoma.

Claim 205 (New): The method of claim 189, wherein the development of hepatocellular carcinoma is selected from the group consisting of growth, proliferation and metastasis of hepatocellular carcinoma.

Claim 206 (New): The method of claim 205, wherein the development of hepatocellular carcinoma comprises growth of hepatocellular carcinoma.

Claim 207 (New): The method of claim 205, wherein the development of hepatocellular carcinoma comprises proliferation of hepatocellular carcinoma.

Claim 208 (New): The method of claim 205, wherein the development of hepatocellular carcinoma comprises metastasis of hepatocellular carcinoma.

Claim 209 (New): A method for screening for biologically active agents that modulate a dysplasia or neoplasia associated with hepatocellular carcinoma, the method comprising:

administering a candidate agent to a transgenic mouse having a genome comprising a stably integrated transgene encoding FGF19 operably linked to a promoter, wherein said transgene results in said mouse developing hepatocellular dysplasia or neoplasia as compared with a control non-transgenic or transgenic mouse; and

determining the extent of development of the hepatocellular carcinoma as indicated by the extent of development of hepatocellular dysplasia or neoplasia in said mouse as compared with the control non-transgenic or transgenic mouse.